Non-technical Abstract

This research is being done to evaluate an approach that uses the transfer of a gene as a method to treat patients with malignant brain tumors called malignant gliomas. Standard treatment for these tumors consists of surgery and/or radiation. The gene transfer approach of this study uses an adenovirus (AdV) from which scientists have removed pieces (viral genes) so that it does not replicate (make more viruses). Viruses that cannot replicate in the body are called vectors. Normal adenoviruses that can replicate cause mild infections and colds in humans. In place of the removed adenovirus genes, a gene from a herpes virus, called the thymidine kinase (tk) gene, has been inserted. This AdV-tk vector is injected into the tumor leading to production of the TK protein in infected tumor cells. The TK protein is what kills cells infected with herpes virus when treated with anti-herpes drugs like valacyclovir. After the AdV-tk injection into the tumor, subjects will be given valacyclovir pills for 14 days. Valacyclovir is a Food and Drug Administration (FDA) approved drug for treating herpes infections. Valacyclovir administration results in the death of cells containing the TK protein. Studies in laboratory animals suggest that the addition of AdV-tk + valacyclovir to surgery or radiation therapy may be beneficial for treating tumors, including brain tumors. The main purpose of this clinical trial is to evaluate the safety of AdV-tk + valacyclovir when used in combination with standard therapy for malignant gliomas. Based on previous experience with this approach in patients with cancer, significant side effects are not expected. However, since this approach has not been used in combination with radiation therapy in people with brain tumors, the trial will evaluate escalating doses of AdV-tk to determine the dose that can be given without causing severe or unmanageable side effects. This dose will then be used in a subsequent study to determine if this approach improves the outcome of treatment for malignant gliomas.